IT **131571-21-6**
RL: PRP (Properties)
(gene for, expression in yeast of, prepn. of human insulin analog with reduced association and)

L58 ANSWER 10 OF 17 HCAPLUS COPYRIGHT 2000 ACS
AN 1991:55873 HCAPLUS
DN 114:55873
TI Ionization behavior of native and mutant insulins: pK perturbation of His B10 and Glu B13 in aggregated species
AU Kaarsholm, Niels C.; **Havelund, Svend**; Ransom, Philip
CS Novo Res. Inst., Bagsvaerd, DK-2880, Den.
SO Arch. Biochem. Biophys. (**1990**), 283(2), 494-500
CODEN: ABBIA4; ISSN: 0003-9861
DT Journal
LA English
AB Upscale titrn. from pH 2.5 to 11.2 is used to probe solvent accessibility of ionizing groups in **Zn**-free prepns. of native and mutant insulins. Stoichiometry and pK values of ionizing groups in the titrn. curves are detd. by iterative curve fitting. Under denaturing conditions, the titrn. curve of human insulin is in good agreement with that predicted from the sum of unperturbed titrns. of the constituent ionizing groups and yields an apparent isoionic point of 5.5. Under nondenaturing conditions where aggregation and pptn. occur, titrns. show that only 5 of 6 carboxylate residues of human insulin ionize in the expected region. Consequently, 1 carboxylate ionization is masked and the apparent isoionic point is located at pH 6.4. Correlation between ionization behavior and patterns of aggregation and soly. is established by titrns. of mutant insulins and of dil. native insulin. Titrn. of an unusually sol. species, B25-Phe .fwdarw. His, shows that pptn. is not responsible for the masked carboxylate ionization of native insulin. Titrns. of mutants B13-Glu .fwdarw. Gln and B9-Ser .fwdarw. Asp show that the masked ionization probably originates from monomer-monomer interactions in the insulin dimer. Thus, the B13-Glu side chain is responsible for the masked carboxylate ionization in aggregated forms of human insulin.
IT **11061-68-0**, Human insulin **72751-52-1** **116094-26-9**
128548-64-1
RL: PROC (Process)
(ionization of, mol. structure in relation to)

L58 ANSWER 11 OF 17 HCAPLUS COPYRIGHT 2000 ACS
AN 1989:186795 HCAPLUS
DN 110:186795
TI Human insulin analogs and injectable solutions containing these analogs and **zinc** ions with prolonged antidiabetic action
IN **Markussen, Jan**; Norris, Klaus; Langkjaer, Lisbeth
PA Novo Industri A/S, Den.
SO Eur. Pat. Appl., 14 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 4

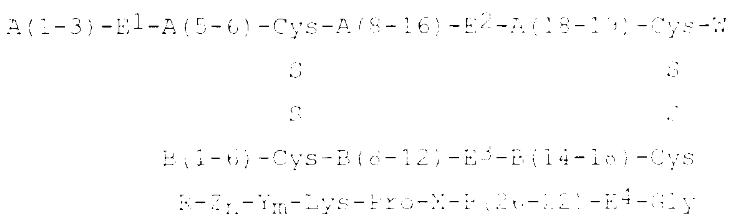
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP [illegible]	A	[illegible]	EP [illegible]	[illegible]
	DK [illegible]	A	[illegible]		
	DK [illegible]	B	[illegible]		

AU 632524	B2	[illegible]		
CN 87104989	A	[illegible]	CN 1987-1[illegible]	[illegible] <--
ZA 8705295	A	[illegible]	ZA 1987-52[illegible]	[illegible] <--
HU 45271	A2	1988[illegible]	HU 1987-[illegible]	1987072[illegible] <--
HU 203371	B	19910729		
DD 273839	A5	19891129	DD 1987-3[illegible]	19870720 <--
US 4946828	A	199008[illegible]	US 1987-75387	19870720 <--
IL 83243	A1	19930114	IL 1987-83243	19870720 <--
AT 99699	E	19940115	AT 1987-306405	19870720 <--
ES 2061504	T3	19941216	ES 1987-306405	19870720 <--
JP 63099096	A2	19880430	JP 1987-180168	19870721 <--
US 5008241	A	19910416	US 1989-424503	19891020 <--

PRAI DK 1986-3470 19860721 <--
DK 1985-1135 19850312 <--
DK 1986-1070 19860310 <--
US 1986-838472 19860311 <--
DK 1987-948 19870225 <--
EP 1987-306405 19870720 <--
US 1987-75550 19870720 <--

OS MARPAT 110:166795

GI



I

AB Insulin derivs. having a pos. charge compared with that of human insulin at neutral pH are used to prep. solns. having prolonged insulin action. These insulin derivs. have the structure I (A and B followed by nos. in parentheses designate peptide fragments of A and B chains, resp.; E1-E4 = Glu, neutral amino acid; X = Thr, Arg, Lys; Y, Z = amino acid in which any side-chain NH2 may be acylated and any side-chain OH may be alkylated; m, n = 0, 1; R = OH, [illegible]; W = [illegible], e.g. Asn, and have [illegible] more charge than human insulin at pH 7. I.e., a basic amino acid in human insulin is substituted in the B27 position and/or a neutral amino acid is inserted in the A4, A17, B1[illegible], and/or B21 position. The C-terminus of the A chain, AsnA21, may be [illegible] [illegible]

7440-66-6 [illegible]

111775-86-1P 111775-87-2P 111775-88-3P
117442-95-2P 117442-96-3P 117442-98-5P
[illegible]

117443-02-4P 117443-03-5P 117443-04-6P
117443-06-8P 117443-07-9P 117443-08-0P
120249-13-0P 120249-15-2P 120249-16-3P
120249-19-6P 120249-21-0P 120249-22-1P
120249-23-2P 120249-24-3P 120249-26-5P
120249-27-6P 120249-29-8P 120249-30-1P
120249-32-3P 120249-33-4P 120249-35-6P
120249-36-7P 120249-37-8P 120249-38-9P
120249-40-3P 120249-41-4P 120249-43-6P
120249-45-8P 120249-46-9P 120249-47-0P
120249-49-2P 120249-50-5P 120249-51-6P
120249-53-8P 120249-55-0P 120249-57-2P
120249-58-3P 120249-59-4P 120249-61-8P
120249-62-9P 120249-63-0P 120249-64-1P
120249-66-3P 120249-68-5P 120249-69-6P
RL: PREP (Preparation)
(prepn. of, as antidiabetics)

IT **11061-68-0DP**, Human insulin, analogs
RL: PREP (Preparation)
(prepn. of, as antidiabetics)

IT **120249-72-1 120249-74-3 120249-75-4**
120249-76-5 120249-77-6 120249-79-8
120249-80-1 120249-81-2
RL: RCT (Reactant)
(transpeptidation of, in prepn. of human insulin analog)

L58 ANSWER 12 OF 17 HCAPLUS COPYRIGHT 2000 ACS
AN 1988:596998 HCAPLUS
DN 109:196998
TI Soluble, prolonged-acting insulin derivatives. II. Degree of protraction, crystallizability and chemical stability of insulins substituted in positions A21, B13, B23, B27 and B30
AU **Markussen, J.**; Diers, I.; Hougaard, P.; Langkjaer, L.; Norris, K.; Snel, L.; Soerensen, A. R.; Soerensen, E.; Voigt, H. O.
CS Novo Res. Inst., Bagsvaerd, 2880, Den.
SO Protein Eng. (**1988**), 2(2), 157-66
CODEN: PRENE9; ISSN: [illegible]
DT Journal
LA English
AB It was previously demonstrated that insulins to which pos. charge has been added by substituting B10 [illegible] with a [illegible], by [illegible] with an arginine or lysine residue, and by blocking the C-terminal carboxyl group of the B-chain by amidation, featured a prolonged absorption from the subcutis of rabbits and pigs after injection in soln. at acidic pH. The phenomenon is ascribed to a low solv. [illegible] with the readiness by which these insulins crystallize at the injection site to [illegible] in the tissue. However, while the [illegible] insulin are [illegible] soluble at pH values [illegible] the B-chain [illegible] this part is [illegible] the [illegible] the [illegible]. In order [illegible] Asn A21 by [illegible] in B13, B23, and B27, challenging the fact that Asn appears [illegible] position throughout the evolution. Pos. [illegible] with glycine, serine, threonine, aspartic acid, histidine and arginine were introduced in this [illegible], with the [illegible]. In the case of [illegible] insulin [illegible] the [illegible]

analog with Asp(B1) glycine showed first-order absorption kinetics in pigs with a half-life of approx. 1 h, independent of the dose given. The day-to-day variation of the absorption of this analog was significantly lower than that of the conventional insulin preparations, a property that might render such an insulin useful in the attempts to improve glucose control in diabetics by a more predictable delivery of basal insulin.

IT **11061-68-0 117442-95-2 117442-97-4**
117442-99-6 117443-02-4 117443-05-7
RL: BIOL (Biological study)
(insulin deriv. precursor, yields of, relative to fermn. biomass)

IT **117442-94-1P 117442-96-3P 117442-98-5P**
117443-00-2P 117443-01-3P 117443-03-5P
117443-04-6P 117443-06-8P 117443-07-9P
117443-08-0P 117443-09-1P 117443-10-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and biol. activity and properties of prolonged-action)

IT **7440-66-6, Zinc**, biological studies
RL: BIOL (Biological study)
(substituted insulin derivs. biol. activity and stability in relation to)

L16 ANSWER 13 OF 17 HCAPLUS COPYRIGHT 2007 ACS
AN 1988:504899 HCAPLUS
DN 109:104954
TI Monomeric insulins obtained by protein engineering and their medical implications
AU Brange, J.; Ribel, U.; Hansen, J. F.; Dodson, G.; Hansen, M. T.; **Havelund, S.**; Melberg, S. G.; Norris, F.; Norris, K.; et al.
CS Novo Res. Inst., Novo Alle, Bagsvaerd, DK-2880, Den.
SO Nature (London) (**1988**), 333(6174), 679-82
CODEN: NATUAS; ISSN: 0028-0836
DT Journal
LA English
AB By single amino-acid substitutions, insulins were prepd. which are essential monomeric at pharmaceutical concns. (0.6 mM) and which have largely preserved their biol. activity. These monomeric insulins are absorbed more rapidly after s.c. injection than the present rapid-acting insulins. They are ideal to mimic a giving diabetic patients a more physiol. plasma insulin profile at the time of meal consumption.

IT **7440-66-6D, Zinc**, complexes with insulin
RL: BSU (Biological study, unclassified)
(bioavailability and biol. activity and self assocn. of)

IT **11061-68-0 11061-68-0D, zinc** complexes
12584-58-6D, zinc complexes **55599-09-2**
111479-48-2 116094-19-0 116094-20-3
116094-21-4 116094-23-6 116094-25-8
116094-26-9 116094-27-0 116094-28-1
116094-29-2
RL: BIOL (Biological study)
[illegible] activity and stability in relation to

L16 ANSWER 14 OF 17 HCAPLUS COPYRIGHT 2007 ACS
AN 1988:222747 HCAPLUS
DN 108:222747
TI [illegible]

were prepd. by substitution with basic amino acids at the termini of the B-chain and by blocking the C-terminal carboxyl group of the B-chain. The isoelec. pH of the insulin is thereby moved from 5.4 towards physiol. levels. Slightly acid solns. of derivs., in which charge has been added in the C-terminus of the B-chain, have a prolonged action in vivo, in particular if the carboxyl group is blocked. The prolonged-acting hydrophilic insulins crystallize instantly when the pH is adjusted to 7. The prolonged action is ascribed to this readiness to crystn. combined with a low solv., which may be further decreased by increased concn. of Zn ions. Hydrophobic insulins have a prolonged action independent of the site of substitution even if the deriv. is sol. at physiol. pH. Some derivs. were prepd. from porcine insulin by tryptic transpeptidation. N-terminal B-chain substituted insulins were prepd. by alkylation of a biosynthetic single-chain insulin precursor, followed by tryptic transpeptidation rendering the double-chain insulin deriv. The obsd. blood glucose lowering in the rabbits implies that neither N- nor C-terminal B-chain substitution results in substantial deterioration of biol. potency. An index for the degree of protraction based on the blood glucose data is used to compare the insulins.

IT **12584-58-6**, Porcine insulin **98743-24-9**
RL: BIOL (Biological study)
(derivs. prepn. from, as prolonged acting derivs.)

IT **113190-02-6P 113190-03-7P 113190-11-7P**
113190-13-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and deprotection of)

IT **74870-09-0P 80449-79-2P 81959-12-8P**
97396-48-0P 110068-63-8P 110068-65-0P
110068-80-9P 110084-28-1P 113189-92-7P
113189-96-1P 113189-97-2P 113190-00-4P
113190-01-5P 113190-07-1P 113190-08-2P
113190-09-3P 113190-10-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and protraction and crystallizability of, as prolonged-acting insulins)

IT **113189-88-1P 113189-89-2P 113189-95-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and transpeptidation of)

IT **113190-14-0P 113314-96-8P 113610-16-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and transpeptination of, with [illegible])

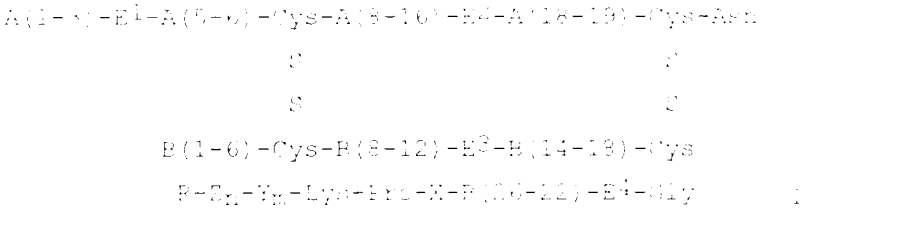
IT **113190-12-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

L[illegible] ANSWER [illegible] OF [illegible] BIOSIS COPYRIGHT [illegible] on STN
AN [illegible]
TI [illegible]
SO [illegible]
AU **Markussen, Jan**
[illegible]
Eur. J. Appl., [illegible].
DOCUMENT TYPE: REVIEW
LA English
[illegible]
[illegible]

[illegible]

IKAI DK 1985-1135 19850312 ---
DK 1986-1070 19860310 ---
EP 1986-301755 19860311 ---
US 1986-838472 19860311 ---
IE 1986-3470 19860721 ---
IN 1987-[illegible] 19870225 ---
US 1987-[illegible] 19870722 ---

GI



AB The title compds. [I; A and B are insulin A- and B-chain peptide fragments, resp.; E1-E4 = Glu, neutral amino acid residue; X = L-Thr, L-Arg, L-Lys; Y, Z = amino acid [illegible]; m, n = [illegible], useful to prep. injectable solns. with prolonged insulin action, were prepd. These preps. may contain Zn2+, preferably at 5-200 mcg./mL. ArgB31-NH2 human insulin was prepd. by transpeptidation of H-Arg-NH2 with [illegible] insulin in the presence of trypsin.

IT 7440-66-6, Zinc, [illegible]
RL: BIOL (Biological study)
(insulin and [illegible], to prep. injectable soln. with prolonged insulin action)

IT 11061-68-0DP, Human insulin, [illegible] 12584-58-6DP, Insulin [illegible], [illegible] 81959-12-8P 110068-58-1P
110068-59-2P 110068-60-5P 110068-61-6P
110068-62-7P 110068-63-8P 110068-64-9P
110068-65-0P 110068-67-2P 110068-68-3P
110068-69-4P 110068-70-7P 110068-72-9P
110068-73-0P 110068-74-1P 110068-75-2P
110068-78-5P 110068-79-6P 110068-80-9P
110068-83-2P 110084-28-1P

AN [illegible]
TI Semisynthesis of human insulin
AU **Markussen, Jan**
CS Novo Ind., Bagsvaerd, Den.
SO Methods Diabetes Res. (**1984**), Volume 1, Issue A, 43-11.
Editor(s): Larner, Joseph; Pohl, Stephen L. Publisher: Wiley, New York, N. Y.
CODEN: 53UDAs
DT Conference
LA English
AB Methods are described for the semisynthesis of human insulin [**11061-68-0**] from porcine insulin [**12584-58-6**], in which des(Ala30) porcine insulin [**39416-73-4**] (formed by 2 different routes) is reacted with various threonine esters. Deprotection of the resulting insulin esters yields human insulin [cont'd. a threonine residue in the carboxyl terminal position of the .beta.-chain].
IT **12584-58-6**
RL: BIOL (Biological study)
(human insulin prepn. from)
IT **74870-09-0P 76688-23-8P 80449-79-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and deprotection of)
IT **7440-66-6DP**, complexes with insulin **11061-68-0DP**, **zinc** complexes **11061-68-0P 39416-73-4DP**, **zinc** complexes
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
IT **39416-73-4**
RL: RCT (Reactant)
(reaction of, with threonine esters)

L[illegible] ANSWER 17 OF 17 HCAPLUS COPYRIGHT 2000 ACS
AN 1983:8177 HCAPLUS
DN 98:8177
TI Stabilized insulin preparations
IN Brange, Jens Jorgen Veilgaard; **Havelund, Svend**
PA Novo Industri A/S, Den.
SO Eur. Pat. Appl., 14 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP [illegible]	A2	19[illegible]	EP [illegible]	[illegible]
	EP [illegible]	A3	[illegible]		
	EP [illegible]	B1	[illegible]		
	R: AT, [illegible]				
	[illegible]	A	[illegible]	[illegible]	[illegible]
	[illegible]	B	[illegible]	[illegible]	[illegible]
	[illegible]	A1	[illegible]		
	[illegible]	A1	[illegible]	[illegible]	[illegible]
	[illegible]	A	[illegible]	[illegible]	[illegible]
	[illegible]	B	[illegible]		
	[illegible]	C	[illegible]		
	[illegible]	A	[illegible]	[illegible]	[illegible]
	[illegible]		[illegible]		

[illegible] A [illegible] [illegible] [illegible]
CH 652031 A 1985[illegible] CH 1982-144[illegible] [illegible]
AT 23208 E [illegible] AT [illegible] [illegible]
FI 78830 B [illegible] FI [illegible] [illegible]
FI 78838 C 1989[illegible]
PRAI GB 1981-7423 19810[illegible] --
DK 1981-4143 19810918 --
EP 1982-[illegible]1207 19[illegible] --
AB Stabilized **zinc** insulin [illegible] prepn. for use in equipment for continuous insulin delivery, comprises a Ca or Mg salt, a preservative, and optionally, a nonionizing osmotic pressure controlling agent and(or) a pH buffering agent which does not form a complex with either Ca or Mg ions in addn. to insulin. Thus, cryst. monocomponent porcine insulin (7.44 g) contg. [illegible].4 **Zn** with a total activity of 200,000 IU was dissolved in 250 mL H2O contg. HCl ([illegible].5 mL N), to this was added 100 mL H2O contg. glycerol and PhOH 6.4 and [illegible].8 g, resp., the pH was adjusted with NaOH to 7.5, and the total vol. increased to 400 mL with H2O. To 100 mL of this soln. was added 29.4 mg CaCl2 and the soln. sterilized by filtration and transferred aseptically to 10 mL vials. The soln. contg. 500 IU insulin/mL in 2 .times. 10-3M soln. CaCl2 had a stability factor [illegible].
IT **11061-68-0D, zinc** complexes
RL: BIOL (Biological study)
(semisynthetic, stable compns. contg. calcium or magnesium salts and)
IT **12584-58-6D, zinc** complexes
RL: BIOL (Biological study)
(stable compn. contg. calcium or magnesium salts)

=> d l59 bib abs hitrn tot

L59 ANSWER 1 OF 26 HCAPLUS COPYRIGHT 2000 ACS
AN 1994:646581 HCAPLUS
DN 121:246581
TI Structural Asymmetry and Half-Site Reactivity in the T to R Allosteric Transition of the Insulin **Hexamer**
AU Brzovic, Peter S.; Choi, [illegible]; [illegible]; Kaarsholm, Niels C.; Dunn, Michael F.
CS Department of Biochemistry, University of California, Riverside, CA, 92521-0129, USA
SO Biochemistry (**1994**), 33(44), 13057-[illegible]
CODEN: BICHAW; ISSN: [illegible]
DT Journal
LA English
AB The **zinc**-insulin **hexamer**, the storage form of insulin in the pancreas, is an allosteric protein [illegible] transitions between three distinct conformational states, designated T6, T3R3, and R6, on the basis of [illegible] properties, [illegible] [illegible] **zinc**-insulin **hexamers** [illegible]

distribution of **hexamer** conformations in favor of the R-state with the order of effectiveness, [illegible]. Anal. of one- and two-dimensional spectra indicate that with wild-type insulin, 2Zn- and Co- give T3R3 species, whereas the B10Asp mutant gives an R6 species. An allosteric model for the insulin T to R transition based on the structural asymmetry model (P. Cuatrecasas, et al. (1974)) is proposed that explains the neg. and pos. allosteric properties of the system, including the role of T3R3 and the action of homotropic and heterotropic effectors.

IT **72751-52-1**, 13B-Glu-human insulin
RL: PRP (Properties)
(insulin **hexamer** structural asymmetry and half-site reactivity in allosteric transition)

L[illegible] ANSWER [illegible] OF [illegible] HCAPLUS COPYRIGHT [illegible] ACS
AN [illegible]:40119 HCAPLUS
DN 121:1195
TI A new structural type of **zinc** insulin observed in a mutant of (A21,Ser)-human insulin
AU Wang, Du-cheng; Zeng, Zhong-hua; Hu, Yong-lin; Markussen, Jon
CS Inst. Biophys., Chin. Acad. Sci., Beijing, 100101, Peop. Rep. China
SO Rept.: Biol. Chem., Proc. Chin. Acad. Symp. **1993**, Meeting Date 1992, 241-4. Editor(s): Du, Yu-zhang; Tam, James P.; Zhang, You-shang. Publisher: ECCOM, Leiden, Neth.
CODEN: 59YOAI
DT Conference
LA English
AB The **hexameric zinc** insulin structure [illegible] in the (A21,Ser)-human insulin crystal represents a new type of T3R3 insulin conformational state (T3Rt3), in which the conformational pattern of the subunits are basically T3R3, except for a nonhelical stretch of B1-B3, but the coordination mode of **zinc ions** in the metal chelate sites adopts a T6-like type, namely 2 **zinc ions** are all on the 3-fold axis and both possess 6 ligands arranged as an octahedral array. In the R3 structure, 6 coordination sites of **zinc ion**(II) are all occupied by the residues of insulin mol. itself, including 3 Asn-B3 and 3 His-B5, which has not yet been observed in other **hexameric** insulin structures. The [illegible] interactions between Asn-B3 and **Zn**(II) should be a significant factor for stabilizing the helical conformation of B1-B9 segment. It seems likely that the T3R3 structure [illegible] the [illegible] B1-B9 conformational transition, which may provide a new model for the investigation of the allosteric transition of insulin. A neutral org. mol., 1,4-dioxane, present in cryst. media is most probably the effector of R6 conformation, which binds to a pocket on the **hexamer** surface and induces the conformational transition from the [illegible] to the R6 conformation.

IT **134091-11-5D**, **hexamers**, [illegible] with **zinc**
RL: [illegible]
[illegible]

L[illegible] ANSWER [illegible] OF [illegible] HCAPLUS COPYRIGHT [illegible] ACS
AN [illegible]:[illegible] HCAPLUS
DN [illegible]
TI Crystallographic Evidence for [illegible] Binding to Two **Zinc** in the T3R3 Human Insulin **Hexamer**
[illegible]

[illegible]

hexamer

[illegible] **zinc ions**

.ANG.. The structure has been refined to a residual of [illegible] using [illegible] independent data points ([illegible]-.ANG. res.). The asym. unit contains [illegible] Tb dimer, and the insulin **hexamer** is generated by the action of the crystallog. 3-fold axis. The conformation of the insulin trimer is nearly identical to that of the Tb **hexamer**, while the other trimer approximates that of the Rb **hexamer**, except for the three N-terminal B-chain residues that adopt an extended rather than an .alpha.-helical conformation. Each of the two **zinc ions**, which lie on the crystallog. 3-fold axis and exhibit two different, disordered coordination geometries, is coordinated by the imidazole groups of three symmetry-related B10 histidine residues. The coordination sphere of the **zinc** in the Tb trimer is either tetrahedral, with the fourth site filled by a chloride **ion**, or octahedral, completed by three water mols. The coordination of the **zinc** in the [illegible]-.ANG. narrow channel in the Rb trimer is tetrahedral, with either a second chloride **ion** or a water mol. completing the coordination sphere. The putative off-axial **zinc** binding sites that result from the T.fwdarw.R transition of monomer II do not contain **zinc ion**, but instead are filled with clusters of ordered water mols. The observation that the T-state trimer contains **zinc** in both tetrahedral and octahedral geometries has important implications for the interpretation of spectroscopic results.

IT **11061-68-0D**, Human insulin, **zinc** complexes, **hexamers**
RL: PRP (Properties)
(crystal structure of, for T3R3 conformation with dual coordination)

IT **7440-66-6D**, **Zinc**, complexes
RL: BIOL (Biological study)
(with human insulin **hexamer** T3R3, crystal structure of)

L59 ANSWER 4 OF 26 HCAPLUS COPYRIGHT 2000 ACS
AN 1994:722 HCAPLUS
DN 120:722
TI Distinction of structural reorganization and ligand binding in the T .tautm. R transition of insulin on the basis of allosteric models
AU Jacoby, Edgar; Krueger, Peter; Karatas, Yasar; Wollmer, Axel
CS Inst. Biochem., Rheinisch-Westfael. Tech. Hochsch., Aachen, Germany
SO Biol. Chem. Hoppe-Seyler (1993), [illegible]
CODEN: BCHSEI; ISSN: 0177-3593
DT Journal
LA English
AB The [illegible] is presented for the T .tautm. R transition of insulin **hexamers** in the presence of phenolic ligands which are based on existing exptl. information. The transition mainly involves residues 1-8 of the B-chain, i.e. 15 [illegible] of the mol., which are extended in the T- and helical in the R-state. The main [illegible] are [illegible] and the transition is subdivided into trimer-wise; the transition of the first trimer is [illegible] compared to the [illegible]; the cooperativity of a trimer with [illegible] is [illegible] by [illegible]; binding of the [illegible], [illegible] the R-state; the [illegible] are [illegible] between two different subunits; binding to [illegible] extends the lifetime of the two other binding sites of a trimer; only trimer-free trimers can undergo transition. The two [illegible] T [illegible] spectroscopic titres. If **zinc** and [illegible] insulin with [illegible] and m-cresol is [illegible] in [illegible] [illegible] [illegible], and [illegible] [illegible] [illegible].

11061-68-0D.

hexamers

... of, in presence of m-cresol and phenol

L1 ANSWER 5 OF 12 HCAPLUS COPYRIGHT ... ACS
AN 1993:260[illegible] HCAPLUS
DN 118:260[illegible]
TI Chemical stability of insulin. 4. Mechanisms and kinetics of chemical transformations in pharmaceutical formulation
AU Brange, Jens
CS Novo Res. Inst., Bagsvaerd, DK-2880, Den.
SO Acta Pharm. Nord. (1992), 4(4), [illegible]
CODEN: APNOEE; ISSN: 1100-1801
DT Journal
LA English
AB Insulin decomps. by a multitude of chem. reactions. It deamidates at two different residues by entirely different mechanisms. In acid, deamidation of AsnA21 is intramolecularly catalyzed by the protonated N-terminal, whereas above pH 6 an intermediate imide formation at residue AsnB3 leads to isoAsp and Asp derivs. The imide formation requires a large rotation around the .alpha.-carbon/peptide carbonyl carbon bond at B3, corresponding to a 10 .ANG. movement of the B-chain N-terminal. The main determinant for the rate of B3 deamidation, as well as for the ratio between the two products formed, is the local conformational structure, which is highly influenced by various excipients and the phys. state of the insulin. An amazing thermolysin-like, autoproteolytic cleavage of the A-chain takes place in rhombohedral insulin crystals, mediated by a concerted catalytic action by several, inter-**hexameric** functional groups and Zn2+. Intermol., covalent crosslinking of insulin mols. occurs via several mechanisms. The most prominent type of mechanism is aminolysis by the N-terminals, leading to isopeptide linkages with the .alpha.-chain side-chain amides of residues GlnA15, AsnA18 and AsnA21. The same type of reaction also leads to covalent crosslinking of the N-terminal in protamine with insulin. Disulfide exchange reactions, initiated by lysis of the A7-B7 disulfide bridge, lead mainly to formation of covalent oligo- and polymers. Activation energy (Ea) for the neutral deamidation and the aminolysis reactions was found to be 80 and 119 KJ/mol, resp.
IT **11061-68-0**, Human insulin **11070-73-8**, Bovine insulin **12584-58-6**, Porcine insulin **62602-61-3**
RL: PRP (Properties)
(degrdn. of, in formulations, kinetics and mechanism of)

L1 ANSWER [illegible] OF 12 HCAPLUS COPYRIGHT ... ACS
AN 1992:645709 HCAPLUS
DN 117:245709
TI Altering the association properties of insulin by amino acid replacement
AU Brems, David N.; Alter, Lois A.; Beckage, Mary J.; Chance, Ronald E.; DiMarchi, Richard D.; Green, Jeffrey; Hayes, Nancy E.; Long, Harold B.; Raught, Alice M.; Shields, James E.; Frank, Brian H.
CS Eli Lilly and Co., Indianapolis, IN, [illegible]
SO Protein Eng. 1992, [illegible]
CODEN: PRENEJ; ISSN: [illegible]
DT Journal
LA English
AB The importance of hydrophobic interactions in the self-assocn. of insulin was established by systematically perturbing the [illegible] of the B-chain. The [illegible] [illegible]

Zn-insulin **hexamer** formation. The [illegible] monomeric insulin through amino acid replacement was investigated with emphasis [illegible] It is demonstrated that self-assoc. of insulin can be drastically altered by substitution of one of two key amino acids.

IT **11061-68-0**, Human insulin **116094-23-6**
133107-40-1 133107-45-6 133107-52-5
133107-64-9 144637-14-9 144637-15-0
RL: PRP (Properties)
(self-assoc. of, C-terminal amino acid role in)

L[illegible] ANSWER 7 OF 10 HCAPLUS COPYRIGHT 2000 ACS
AN [illegible]:4s55a6 HCAPLUS
DN 115:s55a6
TI [illegible] of the phenylalanine B25 side chain in human insulin-receptor and insulin-insulin interactions
AU Mirmira, Raghavendra G.; Tager, Howard S.
CS Dep. Biochem. Mol. Biol., Univ. Chicago, Chicago, IL, [illegible], USA
SO Biochemistry (**1991**), [illegible], [illegible]
CODEN: BICHAW; ISSN: 0006-2960
DT Journal
LA English
AB By using the semisynthesis of both full-length insulin analogs and their des-pentapeptide-(B21-B25)-.alpha.-carboxamide counterparts, the importance of the electronic character and bulk of the position B25 side chain both in directing insulin interaction with its receptor on isolated canine hepatocytes and in determining the ability of insulin to self-assoc. in soln. was examd. Analogs included those in which PheB25 was replaced by cyclohexyl-Ala; Tyr; p-nitro-, p-fluoro-, p-iodo-, or p-amino-Phe; or p-amino-Phe in which the arom. amino function had been acylated by the acetyl, hexanoyl, decanoyl, or 1-adamantaneacetyl group. Findings identify that (a) the .beta.-arom. side chain at position B25 is indeed crit. for high-affinity ligand-receptor interactions, (b) neither electron withdrawal from nor electron donation to the .beta.-arom. ring perturbs ligand-receptor interactions in major ways, (c) considerable latitude is allowed the placement of linear or polycyclic apolar mass at the para position in p-amino-Phe[illegible]-substituted analogs with respect both to receptor binding affinity and [illegible] activity in vitro, and (d) para apolar mass at position B25 is readily accommodated during the self-assoc. of insulin monomers, as assessed by anal. tyrosine radioiodination and spectroscopic anal. [illegible] The data [illegible] are [illegible] in terms of a model for insulin-receptor interactions at the cell membrane in which the position B25 side chain defines the edge of intermol. contact.

IT **103370-34-9 135393-09-8 135393-10-1**
135393-11-2 135393-12-3 135393-13-4
135393-14-5 135393-15-6 135393-16-7
135393-17-8 135393-18-9 135393-19-0
135393-20-3 135393-21-4 135393-22-5
135393-23-6 135393-24-7 135393-25-8
135393-26-9 135393-27-0
RL: PRP (Properties) ; BIOL (Biological study) ; PREP (Preparation)
(receptor binding of, role in [illegible])

[illegible] ANSWER [illegible] OF [illegible] HCAPLUS COPYRIGHT [illegible] ACS
[illegible]
[illegible]

IT Combination

LA English

AB [illegible] insulin-Gly-Lys-phenylethylamide (I) was synthesized, and this novel analog of insulin was fully as active as infant insulin in blood glucose-depressing and mouse convulsion tests. Although the formation of high-mol.-wt. aggregates of human insulin were dependent on Zn2+, the association of I was Zn2+ independent. Thus, the complete B chain and its C-terminus of insulin were not required for its biol. activity, but they were important in the self-association studies of **hexamers** with Zn2+ and in the determination of insulin polymers.

IT **123583-55-1P**

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and biol. activities and properties of)

L54 ANSWER 9 OF 26 HCAPLUS COPYRIGHT 1998 ACS

AN 1991:136174 HCAPLUS

DN 114:136174

TI Insulin association in neutral solutions studied by light scattering

AU Hvidt, Soeren

CS Dep. Chem., Risoe Natl. Lab., Roskilde, DK-4000, Den.

SO Biophys. Chem. (1991), 39(2), 205-15
CODEN: BIOCAZ; ISSN: 0301-4622

DT Journal

LA English

AB Mol. wts. and wt. distributions of sulfated, **Zn**-free, and 2Zn insulins have been measured at pH 7.3 as a function of concn. from 0.1 to 2 mg/mL by use of a combination of light scattering, refractometry, and size-exclusion chromatog. Results show that sulfated insulin is monomeric over the studied concn. range. Wt. av. mol. wts. between those of a monomer and a **hexamer** were found for both **zinc**-free and 2Zn insulins. **Zinc** stabilizes the **hexamer**, and the dimer-**hexamer** equil. const. is approx. 400 times higher in the presence of **Zn** than in its absence. An av. hydrodynamic radius of 5.6 nm, close to the crystallog. size of the insulin **hexamer**, was detd. from dynamic light scattering of 2Zn insulin solns.

IT **24800-07-5D**, **hexamers**, **zinc** complexes

RL: PRP (Properties)
(mol. assocn. of, in neutral solns.)

L54 ANSWER 10 OF 26 HCAPLUS COPYRIGHT 1998 ACS

AN 1991:[illegible]

DN 114:[illegible]

TI The self-association of **zinc**-free human insulin and insulin analog B13-glutamine

AU Hansen, Jorgen F.

CS Biophys. Chem. Lab., H. C. Orsted Inst., Copenhagen, DK-[illegible], Den.

SO Biophys. Chem. 1991, [illegible], 1-[illegible]
CODEN: BIOCAZ; ISSN: [illegible]

DT Journal

LA English

AB The self-assoc. of **Zn**-free human insulin, **Zn**-free insulin analog B13-glutamine, **Zn**-free insulin analog B13-glutamine, and pig human insulin in the millim. concn. range was investigated by measuring the osmotic pressure at pH 7.4 in 0.1 M NaCl, 0.1 M Tris, and 0.1 M phosphate buffer. The self-assoc. was found to be [illegible] Zn [illegible], [illegible] **hexamer**. [illegible] **hexamer**

440-66-6, Zinc

hexamer

IT 72751-52-1
PL: [illegible] (Properties)
[illegible]

L[illegible] ANSWER 11 OF 20 HCAPLUS COPYRIGHT 2[illegible] ACS
AN 1989:625415 HCAPLUS
DN 111:225415
TI Structural transition in the metal-free **hexamer** of protein-engineered [illegible] insulin
AU Wollmer, Axel; Kammerer, Barbara; Stahl, Joerg; Wollberg, Ehrenfried
CS Inst. Biochem., Rheinisch-Westfael. Tech. Hochsch., Aachen, Fed. Rep. Ger.
SO Biol. Chem. Hoppe-Seyler (1989), [illegible], [illegible]
CODEN: BCHSEI; ISSN: 0177-[illegible]
DT Journal
LA English
AB For **hexamer** formation of native insulin the repulsive potential of 6 B13 Glu carboxylate groups coming together in the center is overcome by **Zn** binding to B10 His. Substitution of Gln for Glu in position B13 by site-directed mutagenesis, i.e. replacement of the repelling carboxylates by amide groups, which are offering H-bonding potential, enhances assocn. and allows a metal-free **hexamer** to form. Merely upon addn. of **Zn ions** this **hexamer** undergoes the T6 .rightarrow. T3R3 resp. T6 .rightarrow. R6 structural transition which in the native 2Zn insulin **hexamer** is inducible only by additives like inorg. anions or phenolic compds. [B13 Gln]Insulin **hexamers** are transformed by phenolic compds., but not by anions, even in the absence of any metal. The structural transformation of insulin can thus be brought about in 2 ways. By inorg. **ions** with the **Zn ions** as their points of attack, which preexist in the nontransformed **hexamer**, and by phenol, for which the binding sites close to the Pb histidines come into existence only with the transformation. Therefore transformed and nontransformed **hexamers**, i.e. mols. with helical and extended B chain N-terminus, must be related in a dynamic equil. Phenol acts as a wedge jamming the structure in the transformed state and trapping the **Zn ions**. Combination of transformed 2Zn[B13 Gln]insulin and metal-free native insulin in the absence of additives results in a redistribution of the **Zn ions** in favor of native insulin which is an outcome of the dynamic equil. and also demonstrates an influence of B13 charge on metal binding affinity. Transformation of a single subunit in a **hexamer** would lead to [illegible] mols. in 1 of the 2 layers forming the **hexamer**.
IT 7440-66-6, Zinc, biological studies
PL: BIOL (Biological study)
[illegible]
IT 72751-52-1
PL: [illegible]
[illegible] **hexamer**

L[illegible] ANSWER 12 OF 20 HCAPLUS COPYRIGHT 2[illegible] ACS
AN 1[illegible]:[illegible] HCAPLUS
DN 111:[illegible]
TI [illegible] **hexamer**

the cobalt ions results in dramatic changes in the visible region of the electronic spectrum and thus represents a useful spectroscopic method for studying the T → R transition. Changes in the Co2+ spectral envelope show that the aqua ligand bound with each tetrahedral Co2+ center can be replaced by FCN-, SCN-, OCN-, N3- and NO2-. 19F-NMR expts. show that the binding of m-trifluorocresol stabilizes the R6 state of zinc insulin. The chem. shift and line broadening of the 19F singlet, which arises from the binding, provide a useful probe of the T6 to R6 transition. Due to the appearance of new resonances in the arom. region, the 500 MHz 1H NMR spectrum of the phenol-induced R6 hexamer is readily distinguishable from that of the T6 form. 1H NMR studies show that phenol induces the T6 to R6 transition, both in the (GlnB13)6(Zn2+)2 hexamer and in the metal-free GlnB13 species. Thus, metal binding is not a prerequisite for formation of the R state in this mutant.

IT 7440-66-6D, Zinc, insulin hexamer complexes
RL: PRP (Properties)
(conformational transitions in, spectroscopy of)

IT 72751-52-1D, hexamers, cobalt and zinc complexes
RL: PRP (Properties)
(conformational transitions of, metal binding role in)

L59 ANSWER 13 OF 26 HCAPLUS COPYRIGHT 2006 ACS
AN 1989:400892 HCAPLUS
DN 111:892
TI Studies on the crystal structure of Al-(L-tryptophan) insulin at 2.1 .ANG. resolution
AU Wan, Zhuli; Liang, Dongcai
CS Inst. Biophys., Acad. Sin., Beijing, Peop. Rep. China
SO Sci. Sin., Ser. B (Engl. Ed.) (1988), 31(12), 1416-34
CODEN: SSBSEF; ISSN: 0253-5823
DT Journal
LA English
AB In order to study the biol. effect of alterations to the N-terminus of the insulin A-chain, the crystal structure of Al-(L-Trp) insulin was det'd. It was shown to belong to the trigonal system with space group R3. The parameters of the unit cell were a = b = [illegible] .ANG., c = [illegible] .ANG.. The model was adjusted and refined by using a stereochem.-restrained least squares program, assisted by manual revision of the model based on the difference Fourier map, to a final R-factor of [illegible]. The main chains of both Al-(L-Trp) residues in the asym. unit were well ordered. It was found that the Al-Trp residue of mol. I occupied two distinct positions. From the results of the three-dimensional structure it was proposed that the 4-zinc insulin hexameric form is a [illegible] of two [illegible] insulin [illegible]. The structural details of the insulin [illegible] that [illegible] relationship are discussed.

IT 84134-94-1
RL: [illegible]
(crystal structure of)

L59 ANSWER 14 OF 26 HCAPLUS COPYRIGHT 2006 ACS
AN 1989:[illegible]
DN 111:[illegible]
TI [illegible] zinc [illegible]

conformational transformation of porcine insulin, pro-insulin, and
miniproinsulin **hexamers** miniproinsulin is a pro-insulin analog
wherein the C-peptide is replaced by a dipeptide connecting Gly-A1
and Ala-B30). A nomenclature system is proposed in which the R-**Zn**
and 4-**Zn** crystal forms of the **hexamer** are designated
as the T6 and T3R3 conformations, resp. For all 3 proteins, addn. of SCN-
reduces the rate of sequestering and removal of **zinc ion**
by chelator. The effect of SCN- on the rate of this process sats. at the
same concn. (5 mM) known to induced the T6-to-T3R3 transformation in the
insulin crystal. Under both T6 and T3R3 conditions, crit. stoichiometry
for high-affinity interaction between Zn2+ and each of the 3 proteins is
shown to be 2 mol of Zn2+/mol of protein **hexamer**. Consequently,
the finding that off-axial coordination of Zn2+ via His-B10 and His-B5
residues is of minor importance for the SCN--induced conformational trans-
in each is affirmed. Under T6 conditions, the kinetics of the reactions
between insulin, proinsulin, and miniproinsulin and a variable excess of
terpy are similar and biphasic. The fast phase of each reaction is 1st
order in terpy and 1st order in protein-bound Zn2+ (k = 0.5-1.4 .times.
104 M-1 s-1) and involves the formation of a terpy-Zn2+- protein complex
at each **zinc** sites. The slow phase of each reaction is 1st
order in terpy at low concns. and tends toward a limiting, satd. value at
high terpy concns. In each system, this step involves the rate-limiting
dissocn. of terpy-bound Zn2+ from the protein, followed by the rapid
coordination of a 2nd terpy mol. and formation of (terpy)2Zn2+. Under
T3R3 conditions, the corresponding reactions for the 3 proteins are also
very similar and biphasic. When compared to T6 conditions, the
second-order rate const. of the fast phase is slightly reduced (k =
0.5-0.6 .times. 104 M-1 s-1). The rate of the slow phase is remarkably
reduced (k = 0.05 s-1) and becomes zero order in terpy. The striking
similarity between the kinetic parameters shows that the same process is
rate-limiting for the reaction of terpy with the SCN--induced form of each
protein. The kinetic results indicate a mechanism where one of the two
zinc environments per **hexamer** is transformed by SCN-.
Thus, the slow rate obsd. under T3R3 conditions likely is limited by the
rate of the SCN--induced conformational change. Studies of the rate of
removal of Zn2+ from the insulin **hexamer** under conditions
similar to those which give rise to crystal form provide further evidence
consistent with these conclusions.

IT **7440-66-6D, Zinc,** insulin **hexamer** complexes
11062-03-6D, Proinsulin (pig), **zinc** complexes,
hexamers 12584-58-6D, Porcine insulin, **zinc**
[illegible], **hexamers 119970-48-8**
RL: PRP (Properties)
(conformation of, **zinc**-binding domains in relation to)

L[illegible] ANSWER [illegible] OF [illegible] [illegible] [illegible]
AU [illegible]
TI [illegible]
SO [illegible]
[illegible] [illegible] [illegible], [illegible]
[illegible], [illegible]; [illegible], [illegible]; [illegible], [illegible]
[illegible], [illegible]
[illegible], [illegible]
DT Patent
LA English
FAN.CNT [illegible]
[illegible]

EP [illegible] B1 [illegible]
R: AT, BE, CH, DE, ES, FR, GB, IT, LI, LU, NL, SE
[illegible]
AT 90614 E [illegible]
ES 2067697 A6 [illegible]
DK 8706429 A [illegible]
FK 160460 B [illegible]
DK 160460 C [illegible]
[illegible]
FI 87529 B [illegible]
FI 87529 C [illegible]
NO 8705299 A [illegible]
IRAI DK 1996-1792 [illegible]
EP [illegible]
WO [illegible]

AB The title formulation contains .gtoreq.1 insulins or insulin derivs., which in soln. in the physiol. pH range are predominantly present as monomers, to provide a fast absorption of the insulin administered. Des-pentapeptide (B26-30) porcine insulin-B26-amide (75 mg) was dissolved in 3 mL aq. HCl, then 5 mL of 0.02M NaH2PO4 in 1 phenol was added, NaOH to pH 8.5, and water to 10 mL. This 10 mL soln. was mixed with 10 mL a 5% glycodeoxycholate in 0.15M NaCl, HCl was added to pH 7.5, filled into a bottle which was sealed with a manual atomizer delivering a sp. vol. per puff, and 100 .mu.L (10 IU of insulin activity) was nasally administered through a single puff.. A suppository contg. trisuccinyl human insulin, a nasal formulation contg. sulfated porcine insulin, and a nasal powder contg. des-pentapeptide (B26-30) porcine insulin-B26-amide were also formulated. Monomeric des-pentapeptide (B26-30) porcine insulin-B26-amide was absorbed faster and more reproducibly than **hexameric Zn**-insulin (human) by intranasal administration in rats.

IT **115038-90-9**
RL: PROC (Process)
(nonparenteral formulation of)

IT **39416-70-1**
RL: RCT (Reactant)
(peptide supplier; in nasal glycodeoxycholate formulation)

IT **12584-58-6DP**, Insulin [illegible], [illegible] **97123-35-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and nasal formulation of)

IT **11061-68-0DP**, trisuccinylated
RL: [illegible]
(prepn. of, for nasal administration)

IT **11061-68-0**, Insulin (human)
RL: PROC (Process)
[illegible]

[illegible]

hexamers and **hexameric** [illegible]; in these cases, [illegible]
I was present as specific [illegible] and inhibited [illegible]
[illegible] and Cd2+, monomers and dimers [illegible] to be the only species
present. The significance of these findings, esp. in relation to a role
for Cd2+ in the action of insulin, is discussed.
IT **7440-66-6**, Biological studies
RL: BIOL (Biological study)
(insulin deoxy- [illegible] and Zn2+ binding by)
IT **55599-09-2**
RL: PRP (Properties)
(self-assocn. of, divalent cation effect on)

L59 ANSWER 17 OF 26 HCAPLUS COPYRIGHT [illegible] ACS
AN 1986:192626 HCAPLUS
DN [illegible]
TI Growth of single crystals of [illegible]-Ala]bo pig insulin and their x-ray
crystallographic analysis
AU Niu, Liwen; Chang, Minfa; Wu, Zhili; Liang, [illegible]
CS Inst. Biophys., Acad. Sin., Beijing, Peop. Rep. China
SO Kexue Tongbao (Foreign Lang. Ed.) (**1985**), 30(5), 1109-11
CODEN: KHTBBC; ISSN: [illegible]
DT Journal
LA English
AB Single crystals of [b-Ala]bo pig insulin (I) [**100469-14-5**] were
prepd. and examd. by x-ray crystallog. Crystals were grown in a buffer
contg. citrate and, except for pH, optimal conditions for crystal growth
were similar for those for pig insulin 2-**Zn** rhombohedral
crystals. Isomorphism of I with 2-**Zn** pig insulin was very good
with a difference of only 0.8 in the c-axis. Results indicated that neither
the mode of close packing of the **hexamers** of I in unit cells nor
the essential conformation of the mol. was greatly changed. However, the
intensities of reflections were changed and the diffraction data for I
differed considerably from that of 2-**Zn** pig insulin. Thus,
partial conformation of the I mol. was changed somewhat compared with 2-
Zn pig insulin..
IT **100469-14-5**
RL: [illegible] (Properties)
[illegible]

L59 ANSWER 18 OF 26 HCAPLUS COPYRIGHT 2006 ACS
AN [illegible]
DN [illegible]
TI An application of the rotation function method to the determination of the
crystal structure of (L-Met)B8-insulin-orientation of the molecules in the
unit cell and atomic structural model
AU Pan, Zilin; Tai, Yiqun; Liang, [illegible]
CS Inst. Biophys., Acad. Sin., Beijing, Peop. Rep. China
SO Chinese Physics [illegible] Acta [illegible] 1985, [illegible], [illegible]
CODEN: [illegible]; ISSN: [illegible]
DT Journal
LA Chinese
AB The [illegible] [illegible] the crystal structure
(L-Met)B-insulin. **99102-79-1** using the structure of
rhombohedral 2-**Zn** as a model was carried out. The [illegible]
crystallog. [illegible], which was [illegible] the [illegible], was
[illegible]
hexamer [illegible]

[illegible]

[illegible]

L1: ACT (Exemplar)
[illegible] 1, with **zinc**, [illegible]

[illegible]

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STRUCTURE FILE UPDATES: 26 DEC 2010 HIGHEST RN [illegible]
DICTIONARY FILE UPDATES: 26 DEC 2010 HIGHEST RN [illegible]

[illegible] INFORMATION NOW CURRENT THROUGH [illegible]

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

Structure search limits have been increased. See HELP SLIMIT
for details.

=> d l21 sqide can tot

L21 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2010 ACS
RN 253597-48-7 REGISTRY
CN 2: PN: US6011007 SEQID: 1 unclaimed protein [1/1] (YA INDEX NAME)
FS PROTEIN SEQUENCE
SQL 30
NTE

type	------ location ------		description
unknown	Aaa-1	-	-
unknown	Aaa-3	-	-
[illegible]	Aaa-[illegible]	-	-

SEQ 1 XVXQHLCGSH LVEALYLVCG ERGFFYTPKX
MF Unspecified
[illegible]
CR YA
[illegible] STN Files: CA, CAPLUS, TOXLIT, USPATFULL
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE [illegible]

REFERENCE [illegible]

L21 ANSWER [illegible] REGISTRY [illegible]
RN 253597-47-6 REGISTRY
CN 1: PN: US6011007 SEQID: 1 unclaimed protein [1/1] (YA INDEX NAME)
FS PROTEIN SEQUENCE
SQL 21
NTE

[illegible]	[illegible]	[illegible]	[illegible]

[illegible] REFERENCES IN FILE CA [illegible] TO DATE)
[illegible] REFERENCES IN FILE CAPLUS [illegible] TO DATE)

REFERENCE 1: [illegible]

[illegible]

L6 ANSWER 1 OF [illegible] REGISTRY COPYRIGHT [illegible] ACS
RN **207519-94-6** REGISTRY
CN (1A-21A'),(1B-29B')-Insulin (human), 29B-[N6-[N-[(3.alpha.,[illegible].beta.)-[illegible]-hydroxy-24-oxocholan-24-yl]-L-.alpha.-glutamyl]-L-lysine]- [illegible] (CA INDEX NAME)
FS PROTEIN SEQUENCE
SQL **50,29,21**
NTE multichain
modified (modifications [illegible])

type	------ location ------		description
bridge	Cys-[illegible]	- Cys-[illegible]'	disulfide bridge
bridge	Cys-[illegible]	- Cys-[illegible]'	disulfide bridge
bridge	Cys-6'	- Cys-11'	disulfide bridge

SEQ 1 FVNQHLCGSH LVEALYLVC[illegible] ER[illegible]FFYTP[illegible]K

SEQ 1 GIVEQCCTSI CSLYQLENYC N
MF C[illegible] H[illegible] N[illegible] O[illegible] S6
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL
7 REFERENCES IN FILE CA (1967 TO DATE)
[illegible] REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
7 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: [illegible]

REFERENCE 2: 132:[illegible]702

REFERENCE 3: [illegible]

REFERENCE 4: 1[illegible]:[illegible]

REFERENCE 5: [illegible]

REFERENCE 6: [illegible]

REFERENCE 7: [illegible]

L6 ANSWER [illegible] OF [illegible] REGISTRY COPYRIGHT [illegible] ACS
RN **207519-93-5** REGISTRY
CN Insulin (human), [illegible] (CA INDEX NAME)
FS PROTEIN SEQUENCE
SQL **51,30,21**

SE, 1 FTN,HLGSKH LVEALYLV'S ERJFFYTINT

SEQ 1 GIVE,'''TSI 'SLY,LENYC N
MF C2s1 H4.1 N.5 Os1 S6
CI MAN
SR CA
L' STN FILE: 'A, 'AILUS, T'MLIT, 'IAIA'LL
        1 REFERENCES IN FILE 'A 1'' T' 'ACE'
        1 REFERENCES TO N'N-SPECIFIC DERIVATIVES IN FILE CA
        1 REFERENCES IN FILE 'AILUS (1967 TO DATE)

REFERENCE 1: 123:1435

L' ANSWER 3 OF 5 REGISTRY COPYRIGHT 2[illegible] ACS
RN 207519-92-4 REGISTRY
CN Insulin (human), 29B-[N6-[(3.alpha.,5.beta.,12.alpha.)-3,12-dihydroxy-24-
    oxocholan-24-yl]-L-lysine]- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE
SQ 51,30,21
NTE multichain
    modified (modifications unspecified)

'YP-	------ lo'ation ------	'escription
bridge	Cys-7 - Cys-7'	disulfide bridge
bridge	Cys-19 - Cys-20'	disulfide bridge
bridge	Cys-6' - Cys-11'	disulfide bridge

SEQ 1 FVNQHLCGSH LVEALYLV'S ERJFFYTINT

SEQ 1 GIVEQCCTSI CSLYQLENYC N
MF C281 H421 N65 O80 S6
CI MAN
SR CA
L' STN FILE: 'A, 'AILUS, T'MLIT, 'IAIA'LL
        1 REFERENCES IN FILE 'A 1'' T' 'ACE'
        1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 123:1435

L' ANSWER 4 OF 5 REGISTRY COPYRIGHT 2[illegible] ACS
RN 207519-90-2 REGISTRY
CN Insulin (human), 29B-[N6-[(3.alpha.,5.beta.,12.alpha.)-3,12-dihydroxy-24-
    oxocholan-24-yl]-L-lysine]- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE
SQ 51,30,21
NTE multichain
    modified (modifications unspecified)

'YP-	------ lo'ation ------	'escription
bridge	Cys-7 - Cys-7'	disulfide bridge
bridge	Cys-19 - Cys-20'	disulfide bridge
bridge	Cys-6' - Cys-11'	disulfide bridge

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 129:1028

L69 ANSWER 5 OF 53 REGISTRY COPYRIGHT 2000 ACS
RN 207519-89-9 REGISTRY
CN Insulin (human), 27B-[N6-[4-[(3-[(1-carboxypentyl)amino]propyl)oxy]-1,4-dioxobutyl]-L-lysine]- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE
SQL 51,30,21
NTE multichain
modified (modifications unspecified)

type	------ location ------	description
bridge	Cys-7 - Cys-7'	disulfide bridge
bridge	Cys-19 - Cys-20'	disulfide bridge
bridge	Cys-6' - Cys-11'	disulfide bridge

SEQ 1 FVNQHLCGSH LVEALYLVCG ERGFFYTPKT

SEQ 1 GIVEQCCTSI CSLYQLENYC N
MF C279 H422 N66 O82 S6
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 129:1028

L69 ANSWER 6 OF 53 REGISTRY COPYRIGHT 2000 ACS
RN 207519-88-8 REGISTRY
CN Insulin (human), 27B-[N6-[4-[(3-[(1-carboxypentyl)amino]propyl)oxy]-1,4-dioxobutyl]-L-lysine]- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE
SQL 51,30,21
NTE multichain
modified (modifications unspecified)

type	------ location ------	description
bridge	Cys-7 - Cys-7'	disulfide bridge
bridge	Cys-19 - Cys-20'	disulfide bridge
bridge	Cys-6' - Cys-11'	disulfide bridge

SEQ 1 FVNQHLCGSH LVEALYLVCG ERGFFYTPKT

SEQ 1 GIVEQCCTSI CSLYQLENYC N
MF C279 H421 N65 O83 S6
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL

CN Insulin (human), 29B-[N6-[4-[(4-methoxybenzoyl)amino]-1,4-dioxobutyl]-L-
    lysine]- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE
SQL 51,30,21
NTE multichain
    modified (modifications unspecified)

TYPE	LOCATION		DESCRIPTION
bridge	Cys-7	- Cys-7'	disulfide bridge
bridge	Cys-19	- Cys-20'	disulfide bridge
bridge	Cys-6'	- Cys-11'	disulfide bridge

SEQ 1 FVNQHLCGSH LVEALYLVCG ERGFFYTPKT

SEQ 1 GIVEQCCTSI CSLYQLENYC N
MF C257 H414 N66 O81 S6
CI MAN
CR CA
LC STN Files: CA, CAPLUS, TOXLIT, TOXCENTER
    1 REFERENCES IN FILE CA (1967 TO DATE)
    1 REFERENCES TO NON-CHEMICAL DERIVATIVES IN FILE CA
    1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 129:1026

L66 ANSWER 8 OF 53 REGISTRY COPYRIGHT 2009 ACS
RN 207519-85-5 REGISTRY
CN Insulin (human), 29B-[N6-(4-benzoyl-L-phenylalanyl)-L-lysine]- (9CI) (CA
    INDEX NAME)
FS PROTEIN SEQUENCE
SQL 51,30,21
NTE multichain
    modified (modifications unspecified)

TYPE	LOCATION		DESCRIPTION
bridge	Cys-7	- Cys-7'	disulfide bridge
bridge	Cys-19	- Cys-20'	disulfide bridge
bridge	Cys-6'	- Cys-11'	disulfide bridge

SEQ 1 FVNQHLCGSH LVEALYLVCG ERGFFYTPKT

SEQ 1 GIVEQCCTSI CSLYQLENYC N
MF C257 H414 N66 O81 S6
CI MAN
CR CA
LC STN Files: CA, CAPLUS, TOXLIT, TOXCENTER
    1 REFERENCES IN FILE CA (1967 TO DATE)
    1 REFERENCES TO NON-CHEMICAL DERIVATIVES IN FILE CA
    1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 129:1026

L66 ANSWER 8 OF 53 REGISTRY COPYRIGHT 2009 ACS
RN 207519-84-4 REGISTRY

type	------ location ------		description
[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]

SEQ 1 FVNQHLCGSH LVEALYLVCG ERGFFYTPKT

SEQ [illegible]
[illegible]
MF [illegible]
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXLIT, TOXCENTR
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: [illegible]

REFERENCE 2: [illegible]

REFERENCE 3: [illegible]

REFERENCE 4: [illegible]

[illegible]
RN 207519-82-2 REGISTRY
[illegible]

type	------ location ------		description
[illegible]	Cys-6'	- Cys-11'	[illegible]

CN 1 PYN,HLCGSH LVEALYLVCG ERGFFYTPKT

SEQ 1 GIVEQCCTSI CSLYQLENYC N
MF C166 H247 N65 O74 S6
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1 REFERENCES IN FILE USPATFULL (1971 TO DATE)

REFERENCE 1: 129:1028

L66 ANSWER 11 OF 53 REGISTRY COPYRIGHT 2007 ACS
RN 207519-80-0 REGISTRY
CN Insulin (human), 29B-[N6-(6-cyclohexyl-1-oxopropyl)-L-lysine]- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE
DOL 51,30,21
MIE multichain
modified (modifications unspecified)

type	------ location ------		description
bridge	Cys-7	- Cys-7'	disulfide bridge
bridge	Cys-19	- Cys-20'	disulfide bridge
bridge	Cys-6'	- Cys-11'	disulfide bridge

SEQ 1 FVNQHLCGSH LVEALYLVCG ERGFFYTPKT

SEQ 1 GIVEQCCTSI CSLYQLENYC N
MF C166 H247 N65 O74 S6
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1 REFERENCES IN FILE USPATFULL (1971 TO DATE)

REFERENCE 1: 129:1028

L66 ANSWER 11 OF 53 REGISTRY COPYRIGHT 2007 ACS
RN 207519-79-7 REGISTRY
CN Insulin (human), 29B-[N6-(6-cyclohexyl-1-oxopropyl)-L-lysine]- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE
DOL 51,30,21
MIE multichain
modified (modifications unspecified)

type	------ location ------		description
bridge	Cys-7	- Cys-7'	disulfide bridge
bridge	Cys-19	- Cys-20'	disulfide bridge
bridge	Cys-6'	- Cys-11'	disulfide bridge

CF CA
LC STN Files: CA, CAPLUS, TOXLIT, TOXCENTER
1 REFERENCE IN FILE CA (1967 TO DATE)
1 REFERENCE TO 1 NON-SPECIFIC DERIVATIVE IN FILE CA
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 129:10226

L[illegible] ANSWER 14 OF [illegible] REGISTRY COPYRIGHT 2[illegible] ACS
RN 207519-78-6 REGISTRY
CN Insulin (human), 29B-[N6-(carboxymethyl)-L-lysine]- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE
SQL 51,30,21
NTE multichain
modified (modification unspecified)

type	------ location ------		annotation
bridge	Cys-7	- Cys-7'	disulfide bridge
bridge	Cys-19	- Cys-20'	disulfide bridge
bridge	Cys-7'	- Cys-11'	disulfide bridge

SEQ 1 FVNQHLCGSH LVEALYLVCG ERGFFYTPKT

SEQ 1 GIVEQCCTSI CSLYQLENYC N
MF C265 H395 N65 O78 S6
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXLIT, TOXCENTER
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 129:10226

L[illegible] ANSWER [illegible] OF [illegible] REGISTRY COPYRIGHT 2[illegible] ACS
RN 186003-66-7 REGISTRY
CN Insulin (human), 29B-[N6-(1-oxohexadecyl)-L-lysine]- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE
SQL 51,30,21
NTE multichain
modified (modification unspecified)

type	------ location ------		annotation
bridge	Cys-7	- Cys-7'	disulfide bridge
bridge	Cys-19	- Cys-20'	disulfide bridge
bridge	Cys-7'	- Cys-11'	disulfide bridge

SEQ 1 FVNQHLCGSH LVEALYLVCG ERGFFYTPKT

SEQ 1 GIVEQCCTSI CSLYQLENYC N

REFERENCE 2: [illegible]

REFERENCE 3: [illegible]

REFERENCE 4: [illegible]

REFERENCE 5: [illegible]

REFERENCE 6: [illegible]

REFERENCE 7: [illegible]

REFERENCE 8: [illegible]

REFERENCE 9: [illegible]

REFERENCE 10: [illegible]

L60 ANSWER 16 OF 57 REGISTRY [illegible]
RN 175895-36-0 REGISTRY
CN Insulin (human), 28B-[N6-(1-oxo[illegible]-L-lysine]- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE
SQL 51,30,21
NTE multichain
modified (modifications unspecified)

type	------ location ------	description
bridge	Cys-7 - Cys-7'	disulfide bridge
bridge	Cys-19 - Cys-19'	disulfide bridge
bridge	Cys-6' - Cys-11'	disulfide bridge

CRN 1 [illegible]

CA 1 [illegible]
DR 270588-46-0
MF C271 H409 N65 O78 S6
SR CA
LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL
1' REFERENCES IN FILE 'A' [illegible]
1 REFERENCES IN FILE 'CAPLUS' [illegible]
1 REFERENCES IN FILE 'TOXLIT' [illegible]

REFERENCE 1: [illegible]

REFERENCE 2: [illegible]

REFERENCE 3: [illegible]

REFERENCE 4: [illegible]

REFERENCE 5: [illegible]

[illegible]

REFERENCE 11: [illegible]

L[illegible] ANSWER 17 OF [illegible] REGISTRY COPYRIGHT [illegible] ACS
RN 169535-38-0 REGISTRY
CN 1-9-Peptide (synthetic 9-amino acid extension) fusion protein with .alpha.-factor receptor (Saccharomyces cerevisiae leader peptide) fusion protein with peptide (synthetic 5-amino acid) fusion protein with insulin B-chain (1-arginine,[illegible]-arginine) (human) ([illegible]) (CA INDEX NAME)
OTHER NAMES:
CN 19: PN: US6011007 SEQID: 4[illegible] claimed protein
FS PROTEIN SEQUENCE
SQL 146

SEQ 1 MRFPSIFTAV LFAASSALAA PVNTTTEDET AQIPAEAVIG YSDLEGDFDV
51 AVLPFSNSTN NGLLFINTTI ASIAAKEEGV SMAKREEAEA EARFVNQHL
101 CGSHLVEALY LVCGERGFFY TPKTRG[illegible] [illegible] LENYCN
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:73648

REFERENCE 2: 123:322102

L60 ANSWER 18 OF 53 REGISTRY COPYRIGHT [illegible] ACS
RN 169535-36-8 REGISTRY
CN 1-8-Peptide (synthetic) fusion protein with .alpha.-factor receptor (Saccharomyces cerevisiae leader peptide) fusion protein with peptide (synthetic 5-amino acid) fusion protein with insulin B-chain (1-arginine) (human) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 21: PN: US6011007 SEQID: 48 claimed protein
FS PROTEIN SEQUENCE
SQL 145

SEQ 1 MRFPSIFTAV LFAASSALAA PVNTTTEDET AQIPAEAVIG YSDLEGDFDV
51 AVLPFSNSTN NGLLFINTTI ASIAAKEEGV SMAKREEAEA EARFVNQHLC
101 GSHLVEALYL VCGERGFFYT [illegible]
MF [illegible]
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL
[illegible] REFERENCES IN FILE CA ([illegible] TO DATE)
[illegible] REFERENCES IN FILE CAPLUS ([illegible] TO DATE)

REFERENCE 1: [illegible]

REFERENCE 2: [illegible]

L[illegible] ANSWER 19 OF [illegible] REGISTRY COPYRIGHT [illegible] ACS
RN 169535-34-6 REGISTRY
CN Receptor, .alpha.-factor (Saccharomyces cerevisiae [illegible]) [illegible]
[illegible]

MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:73644

REFERENCE 2: 123:322102

L60 ANSWER 21 OF 24 REGISTRY COPYRIGHT 2003 ACS
RN 169535-30-2 REGISTRY
CN Peptide (Saccharomyces cerevisiae cytochrome c oxidase subunit I precursor
protein with peptide (synthetic 5-amino acid) fusion protein with insulin
(human A-chain) fusion protein with insulin (human plus B-chain) (9CI)
(CA INDEX NAME)
OTHER NAMES:
CN 16: PN: WO9611687 SEQID: 96 claimed protein
FS PROTEIN SEQUENCE
SQL 102

SQ [illegible]
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

[illegible]

OTHER NAMES:
CN 11: PN: US6011007 SEQID: 88 claimed protein
FS PROTEIN SEQUENCE
SQL 140

SEQ 1 MKRISIFTAV LFAASRGLAA PVNTTTEDET AQIPAEAVIG YSDLEGDFDV
61 AVLPFSNSTN NGLLFINTTI ASIAAKEEGV SLEKREAEAE AGGHLTAGRR
121 TLTSGERFFV TTEKSIAKGV KELPTSLMQK YGRRSGLTFS

MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:73648

REFERENCE 2: 123:322102

L60 ANSWER 23 OF 53 REGISTRY COPYRIGHT 2000 ACS
RN 169535-26-6 REGISTRY
CN Protein (Saccharomyces cerevisiae pEAI + pEAI-LysB28Pro insB1-phe[gly], fusion protein with peptide (synthetic 5-amino acid) fusion protein with insulin A-chain [21-glycine] (human) fusion protein with insulin B-chain [3-threonine] (human) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 9: PN: US6011007 SEQID: 80 claimed protein
FS PROTEIN SEQUENCE
SQL 104

SEQ 1 MKAFLVLSL IGFVWASVT GESLVDILK EGLIAEPTT LANVAMAKRE
61 VTQHLCGSHL VEALYLVCGE RGFFYTPKSD DARGIVEQCC TSICSLYQLE
101 NYCG
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:73648

REFERENCE 2: 123:322102

L60 ANSWER 24 OF 53 REGISTRY COPYRIGHT 2000 ACS
RN 169535-24-4 REGISTRY
CN Protein (Saccharomyces cerevisiae pEAI + pEAI-LysB28Pro insB1-phe[gly], fusion protein with peptide (synthetic 5-amino acid) fusion protein with insulin A-chain [21-glycine] (human) fusion protein with insulin B-chain [3-threonine] (human) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 10: PN: US6011007 SEQID: 84 claimed protein
FS PROTEIN SEQUENCE
SQL 104

SEQ 1 MKAFLVLSL IGFVWASVT GESLVDILK EGLIAEPTT LANVAMAKRE

REFERENCE [illegible]

L[illegible] ANSWER [illegible] REGISTRY [illegible]
RN 169535-22-2 REGISTRY
CN Peptide (Saccharomyces cerevisiae synthetic signal [illegible]) fusion protein with peptide (synthetic [illegible]-amino acid) fusion protein with insulin A-chain (21-alanine) (human) fusion protein with insulin B-chain (3-aspartic acid) (human) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN [illegible]
FS PROTEIN SEQUENCE
SQL 104

SEQ [illegible]
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXLIT, TOXCENTER
[illegible] REFERENCES IN FILE CA [illegible]
[illegible] REFERENCES IN FILE CAPLUS [illegible]

REFERENCE [illegible]

REFERENCE [illegible]

L63 ANSWER 26 OF 53 REGISTRY COPYRIGHT 2008 ACS
RN 169535-20-0 REGISTRY
CN Peptide (Saccharomyces cerevisiae synthetic signal [illegible]) fusion protein with peptide (synthetic [illegible]-amino acid) fusion protein with insulin A-chain (21-alanine) (human) fusion protein with insulin B-chain (3-aspartic acid) (human) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 2: PN: US6011007 SEQID: 21 claimed protein
FS PROTEIN SEQUENCE
SQL 104

SEQ [illegible]
MF [illegible]
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXLIT, TOXCENTER
[illegible] REFERENCES IN FILE CA [illegible]
[illegible] REFERENCES IN FILE CAPLUS [illegible]

REFERENCE [illegible]

REFERENCE [illegible]

L[illegible] ANSWER [illegible] REGISTRY [illegible]
RN 169535-18-6 REGISTRY
CN [illegible]

FS PROTEIN SEQUENCE
SQL **140**

SEQ 1 MKFISIFTAV LFAASALAAP VNTTTEDET AQIPAEAVIG YSDLEGDFDV
51 AVLPFSNSTN NGLLFINTTI ASIAAKEEGV SLEKREADAE [illegible]
101 YLVCTERGFF YTPKSRDAKG IVEQCCTSIC SLYQLENYCN
MF Unspecified
CI MAN
OS [illegible]
DT [illegible] Files: [illegible], CAPLUS, TOXLIT, USPATFULL
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 142:73648

REFERENCE 2: 134:[illegible]

L60 ANSWER 28 OF 53 REGISTRY [illegible]
RN **169535-16-4** REGISTRY
CN Peptide (Saccharomyces cerevisiae clone pAK1ss synthetic signal
LaC21(spx3) fusion protein with 1-(B-insulin (human clone pAK1ss B-Val1
fusion protein with peptide (synthetic B-amino acid fusion protein with
B-insulin (human clone pAK1ss A-Chain)) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 3: PN: US6011007 SEQID: 15 claimed protein
CN Peptide (Saccharomyces cerevisiae clone pAK1ss synthetic signal
LaC21(spx3) fusion protein with proinsulin deletion derivative (30-serine,
31-aspartic acid, 32-aspartic acid, 33-alanine, 34-lysine) (human clone
pAK1ss isoform MIS)
FS PROTEIN SEQUENCE
SQL **104**

SEQ 1 MKAVFLVLSL IGFCWAQPVT SDENSVEIPE EGLIAENTT LANVAMAKEF
51 VNQHLCGSHL VEALYLVCGE RGFFYTPKSD DAKGIVEQCC TSICSLYQLE
101 NYCN
MF Unspecified
CI MAN
OS CA
DT [illegible] Files: CA, CAPLUS, TOXLIT, USPATFULL
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 142:73648

REFERENCE 2: 134:322102

L[illegible] ANSWER [illegible] REGISTRY [illegible]
RN **169148-75-8** REGISTRY
CN [illegible]
OTHER CA INDEX NAMES:
CN [illegible]
[illegible]

bridge	Cys-7'	- Cys-1'	disulfide bridge

SEQ 1 REAEAEARFV N[illegible]HLCGSHLV EALYLVCGER GFFYTPK

SEQ 1 TRGIVEQCCT SICSLYQLEN YCN
MF C54 H76 N18 O17 S6
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXLIT, TOXCENTER
2 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: [illegible]

REFERENCE 2: [illegible]

L60 ANSWER 59 OF 59 REGISTRY COPYRIGHT 2007 ACS
RN 169148-74-7 REGISTRY
CN (1A-21A),(1B-29B)-Insulin (human), NA-(L-threonyl-L-arginyl)-NB-(L-alpha-glutamyl-L-alpha-glutamyl-L-alanyl-L-alpha-glutamyl-L-alanyl-L-alpha-glutamyl-L-alanyl-L-arginyl)- (9CI) (CA INDEX NAME
OTHER CA INDEX NAMES:
CN (1A-21A),(1B-29B)-Insulin (human), NA-(N2-L-threonyl-L-arginyl)-NB-[N2-[N-[N-[N-[N-[N-[N-L-alpha-glutamyl-L-alpha-glutamyl-L-alanyl]-L-alpha-glutamyl]-L-alanyl]-L-alpha-glutamyl]-L-alanyl]-L-arginyl]-
FS PROTEIN SEQUENCE
SQL 60,37,23
NTE multichain
modified (modifications unspecified)

type	------ location ------		description
bridge	Cys-15	- Cys-9'	disulfide bridge
bridge	Cys-27	- Cys-22'	disulfide bridge
bridge	Cys-9'	- Cys-1'	disulfide bridge

SEQ 1 REAEAEARFV N[illegible]HLCGSHLV EALYLVCGER GFFYTPK

SEQ 1 TRGIVEQCCT SICSLYQLEN YCN
MF [illegible]
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXLIT, TOXCENTER
[illegible]

REFERENCE [illegible]

REFERENCE [illegible]

L60 ANSWER 59 OF 59 REGISTRY COPYRIGHT 2007 ACS
RN 169148-73-6 REGISTRY
[illegible]

type	------ location ------		description
bridge	Cys-7	- Cys-7'	disulfide bridge
bridge	Cys-19	- Cys-20'	disulfide bridge
bridge	Cys-6'	- Cys-11'	disulfide bridge

SEQ 1 FVNQHLCGSH LVEALYLVCG ERGFFYTPKT

SEQ 1 GIVEQCCTSI CSLYQLENYC N
MF C256 H428 N66 O52 S6
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXLIT, TOXCAFULL
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 120:72648

REFERENCE 2: 125:222200

L60 ANSWER 82 OF 83 REGISTRY COPYRIGHT 2003 ACS
RN 169148-72-5 REGISTRY
CN Insulin (human), 29B-[N6-[(2-alpha-L-arabinofuranosyl-4-O-beta-D-galactopyranosyl-D-arabino-hexitol-1-yl)-L-lysine]- (4CI) (CA INDEX NAME)
CT PROTEIN SEQUENCE
SQL 51,30,21
NTE multichain
modified (modifications unspecified)

type	------ location ------		description
bridge	Cys-7	- Cys-7'	disulfide bridge
bridge	Cys-19	- Cys-20'	disulfide bridge
bridge	Cys-6'	- Cys-11'	disulfide bridge

SEQ 1 FVNQHLCGSH LVEALYLVCG ERGFFYTPKT

SEQ 1 GIVEQCCTSI CSLYQLENYC N
MF C281 H421 N65 O79 S6
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXLIT, TOXCAFULL
3 REFERENCES IN FILE CA (1967 TO DATE)
3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 120:72648

REFERENCE 2: 125:222200

REFERENCE 3: 125:222200

L60 ANSWER 83 OF 83 REGISTRY COPYRIGHT 2003 ACS
RN 169148-71-4 REGISTRY
CN Insulin (human), 29B-[N6-[(2-O-alpha-D-xylofuranosyl-alpha-L-arabinofuranosyl)-L-lysine]- (4CI) (CA INDEX NAME)
CT PROTEIN SEQUENCE
SQL 51,30,21

SEQ 1 FVNQHLCGSH LVEALYLVCG ERGFFYTPKT

SEQ 1 GIVEQCCTSI CSLYQLENYC N
MF C274 H422 N66 O82 S6
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE [illegible]

REFERENCE 1: 132:73648

REFERENCE 2: 133:32262

L6 ANSWER 54 OF 56 REGISTRY COPYRIGHT 2008 ACS
RN 169148-69-0 REGISTRY
CN [illegible]
FS PROTEIN SEQUENCE
SQL 51,30,21
NTE multichain
modified (modifications unspecified)

---

type	------ location ------	description
[illegible]	[illegible]	[illegible]

SEQ 1 FVNQHLCGSH LVEALYLVCG ERGFFYTPKT

SEQ 1 GIVEQCCTSI CSLYQLENYC N
MF C274 H422 N66 O82 S6
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE [illegible]

REFERENCE 1: 132:73648

REFERENCE 2: 133:32262

L6 ANSWER 55 OF 56 REGISTRY COPYRIGHT 2008 ACS
RN 169148-69-0 REGISTRY
CN [illegible]
FS PROTEIN SEQUENCE
SQL 51,30,21
NTE multichain
modified (modifications unspecified)

---

type	------ location ------	description
[illegible]	[illegible]	[illegible]

CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL
                2 REFERENCES IN FILE CA (1967 TO DATE)
                2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: [illegible]

REFERENCE 2: [illegible]

L60 ANSWER 56 OF 56 REGISTRY COPYRIGHT [illegible] ACS
RN **169148-68-9** REGISTRY
CN Insulin (human), 29Ala-[N6-[N-(1-oxo[illegible]-L-alpha-glutamyl]-L-lysine]- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE
SQL **51,30,21**
NTE multichain
     modified (modifications unspecified)

type	------ location ------	description
bridge	Cys-7 - Cys-7'	disulfide bridge
bridge	Cys-19 - Cys-19'	disulfide bridge
bridge	Cys-6' - Cys-11'	disulfide bridge

SEQ 1 FVNQHLCGSH LVEALYLVCG ERGFFYTPKT

SEQ 1 GIVEQCCTSI CSLYQLENYC N
MF C276 H410 N66 O81 S6
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL
                3 REFERENCES IN FILE CA (1967 TO DATE)
                1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
                3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: [illegible]

REFERENCE 2: 129:102a

REFERENCE 3: [illegible]

L60 ANSWER 57 OF 56 REGISTRY COPYRIGHT 2001 ACS
RN **169148-67-8** REGISTRY
CN Insulin (human), 29Ala-[N6-[N-(1-oxo[illegible]-L-alpha-glutamyl]-L-lysine] - (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE
SQL **51,30,21**
NTE multichain
     modified (modifications unspecified)

type	------ location ------	description
bridge	Cys-7 - Cys-7'	disulfide bridge
bridge	Cys-19 - Cys-19'	disulfide bridge
bridge	Cys-6' - Cys-11'	disulfide bridge

[illegible] REFERENCES IN FILE CA [illegible] TO DATE
[illegible] REFERENCES IN FILE CAPLUS [illegible] TO DATE

REFERENCE 1: [illegible]

REFERENCE 2: [illegible]

L[illegible] ANSWER [illegible] OF [illegible] REGISTRY [illegible]
AN 169148-66-7 REGISTRY
CN Insulin (human), 29B-[N6-[2- 4-oxy[illegible]-3,5-diiodophenyl -3,5-diiodo-L-tyrosyl]-L-lysine]- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE
MF [illegible]
LC STN Files: [illegible]
Modified residues unspecified

type	location	description
bridge	Cys-7 - Cys-7'	disulfide bridge
bridge	Cys-19 - Cys-20'	disulfide bridge
bridge	Cys-6' - Cys-11'	disulfide bridge

SEQ 1 FVNQHLCGSH LVEALYLVCG ERGFFYTPK

SEQ 1 GIVEQCCTSI CSLYQLENYC N
MF C272 H392 I4 N66 O80 S6
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXLIT, [illegible]
3 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:73648

REFERENCE [illegible]

REFERENCE 3: 123:322102

L[illegible] ANSWER [illegible] OF [illegible] REGISTRY [illegible]
AN 169148-65-6 REGISTRY
CN Insulin (human), 29B-[N6-[[4-(4-hydroxy-3,5-diiodophenoxy)-3,5-diiodophenyl]acetyl]-L-lysine]- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE
MF [illegible]
LC STN Files: [illegible]
Modified residues unspecified

type	location	description
bridge	Cys-7 - Cys-7'	disulfide bridge
bridge	Cys-19 - Cys-20'	disulfide bridge
bridge	Cys-6' - Cys-11'	disulfide bridge

[illegible]

REFERENCE 1: [illegible]

REFERENCE 2: [illegible]

REFERENCE 3: [illegible]

L[illegible] ANSWER 4 OF 5 REGISTRY COPYRIGHT [illegible]
RN 169148-64-5 REGISTRY
CN (1A-21A),(1B-10B)-Insulin (human), 1-N-(N-L-[illegible]-L-lysine)-
(9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE
SQL 50,29,21
NTE multichain
Modified at multiple sites

type	------ Location ------	Acetylation
bridge	Cys-7 - Cys-7'	disulfide bridge
bridge	Cys-19 - Cys-20'	disulfide bridge
bridge	Cys-6' - Cys-11'	disulfide bridge

SEQ 1 FVNQHLCGSH LVEALYLVCG ERGFFYTPK

SEQ 1 GIVEQCCTSI CSLYQLENYC N
DR 270588-28-8
MF C269 H406 N64 O76 S6
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXLIT, TOXCENTER
11 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
11 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 133:9108

REFERENCE 2: [illegible]

REFERENCE 3: 132:209852

REFERENCE 4: [illegible]

REFERENCE 5: 131:106812

REFERENCE 6: [illegible]

REFERENCE 7: [illegible]

REFERENCE 8: [illegible]

REFERENCE 9: [illegible]

REFERENCE 10: [illegible]

L[illegible] ANSWER 5 OF 5 REGISTRY COPYRIGHT [illegible]
RN 169148-63-4 [illegible]

50,29,21

Type	Location	Description
[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]

[illegible]

SEQ 1 FVN,HLC[illegible]

SEQ 1 GIVEQCCTSI SLYQLENYC N
DR 20[illegible]
MF C267 H402 N64 O76 S6
CI MAN
SR CA
[illegible]

REFERENCE 1: [illegible]

REFERENCE 2: [illegible]

REFERENCE 3: [illegible]

REFERENCE 4: [illegible]

REFERENCE 5: [illegible]

REFERENCE 6: [illegible]

REFERENCE 7: [illegible]

REFERENCE 8: [illegible]

REFERENCE 9: [illegible]

REFERENCE 10: [illegible]

L60 ANSWER 42 OF [illegible]
RN 169148-62-3
CN Insulin (human), 29B-[N6-(1-oxooctyl)-L-lysine]- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE
SQL 51,30,21
NTE [illegible]

Type	Location	Description
[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]

[illegible]

7 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:[illegible]

REFERENCE 2: 131:[illegible]

REFERENCE 3: 130:[illegible]

REFERENCE 4: 129:[illegible]

REFERENCE 5: 125:[illegible]

REFERENCE 6: 124:127039

REFERENCE 7: 124:[illegible]

L60 ANSWER 43 OF 58 REGISTRY COPYRIGHT 2000 ACS
RN 169148-61-2 REGISTRY
CN Insulin (human), NA-[(1,1-dimethylethoxy)carbonyl]-NB-[(1,1-dimethylethoxy)carbonyl]- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE
SQL 50,29,21
NTE multichain
modified (modifications unspecified)

type	------ location ------	description
bridge	Cys-7 - Cys-7'	disulfide bridge
bridge	Cys-19 - Cys-19'	disulfide bridge
bridge	Cys-6' - Cys-11'	disulfide bridge

SEQ 1 FVNQHLCGSH LVEALYLVCG ERGFFYTPK

SEQ 1 GIVEQCCTSI CSLYQLENYC N
[illegible]
NT MAN
SR CA
LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL
2 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCE IN FILE CAPLUS (PRIORITY OR EQUIVALENT IN file X)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:[illegible]

REFERENCE 2: [illegible]

L60 ANSWER 44 OF 58 REGISTRY COPYRIGHT 2000 ACS
RN 169148-60-1 REGISTRY
CN [illegible]
(CA INDEX NAME)
FS PROTEIN SEQUENCE
SQL 50,29,21
NTE multichain
[illegible]

MF [illegible]
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXLIT, TOXCENTER
4 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
4 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: [illegible]

REFERENCE 2: [illegible]

REFERENCE 3: [illegible]

REFERENCE 4: 123:322102

L66 ANSWER 49 OF 53 REGISTRY [illegible]
RN 169148-59-8 REGISTRY
CN Insulin (human), 29B-[N6-[(octyloxy)carbonyl]-L-lysine]- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE
SQL 50,29,21
NTE multichain
modified (modifications unspecified)

type	------ location ------		description
bridge	Cys-7	- Cys-7'	disulfide bridge
bridge	Cys-19	- Cys-20'	disulfide bridge
bridge	Cys-6'	- Cys-11'	disulfide bridge

SEQ 1 FVNQHLCGSH LVEALYLVCG ERGFFYTPK

SEQ 1 GIVEQCCTSI CSLYQLENYC N
NE [illegible]
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXLIT, TOXCENTER
4 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
4 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: [illegible]

REFERENCE 2: [illegible]

REFERENCE 3: [illegible]

L66 ANSWER 50 OF 53 REGISTRY [illegible]
RN 169148-58-7 REGISTRY
CN [1A-21A],[1B-29B]-Insulin (human), 6B-[N6-[(octyloxy)carbonyl]-L-lysine]- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE
SQL 50,29,21

SEA [illegible]
MF [illegible]
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXLIT, TOXLIT2

REFERENCE 1: [illegible]

REFERENCE 2: [illegible]

REFERENCE 3: [illegible]

REFERENCE 4: [illegible]

REFERENCE 5: [illegible]

REFERENCE 6: [illegible]

L[illegible] ANSWER 47 OF [illegible] REGISTRY [illegible]
RN 169148-57-6 REGISTRY
CN (1A-21A),(1B-29B)-Insulin (human), [illegible]-L-lysine]- (9CI)
(CA INDEX NAME)
FS PROTEIN SEQUENCE
SQL 50,29,21
NTE multichain
modified (modifications unspecified)

type	------ location ------	description
bridge	Cys-7 - Cys-7'	disulfide bridge
bridge	Cys-19 - Cys-[illegible]'	disulfide bridge
bridge	Cys-6' - Cys-11'	disulfide bridge

SEQ 1 FVNQHLCGSH LVEALYLVCG ERGFFYTPK

SEQ 1 GIVEQCCTSI CSLYQLENYC N
[illegible]
SR CA
LC STN Files: CA, CAPLUS, TOXLIT, TOXLIT2

REFERENCE 1: [illegible]

REFERENCE 2: [illegible]

REFERENCE 3: [illegible]

REFERENCE 4: [illegible]

[illegible]

type	------ location ------	description
bridge	Cys-7 - Cys-[illegible]	disulfide bridge
bridge	Cys-13 - Cys-[illegible]	disulfide bridge
bridge	Cys-[illegible] - Cys-[illegible]	disulfide bridge

SEQ 1 FVNQHLCGSH LVEALYLVCG ERGFFYTPKT

SEQ 1 GIVEQCCTSI CSLYQLENYC N

MF C263 H394 N64 O76 S6

CI MAN

SR CA

LC STN Files: CA, CAPLUS, TOXLIT, TOXFILE

(1 REFERENCES IN FILE CA [illegible] TO DATE)

(1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA)

(1 REFERENCES IN FILE CAPLUS [illegible] TO DATE)

REFERENCE 1: [illegible]

REFERENCE 2: 129:1028

REFERENCE [illegible]

L60 ANSWER 49 OF 53 REGISTRY COPYRIGHT 2006 ACS

RN **169148-55-4** REGISTRY

CN (1A-21A),(1B-29B)-Insulin (human), 29B-[N6-(1-oxodecyl)-L-lysine]- (9CI)

(CA INDEX NAME)

FS PROTEIN SEQUENCE

SQL **50,29,21**

NTE multichain

modified (modifications unspecified)

type	------ location ------	description
bridge	Cys-7 - Cys-[illegible]	disulfide bridge
bridge	Cys-[illegible] - Cys-[illegible]	disulfide bridge
bridge	Cys-[illegible] - Cys-[illegible]	disulfide bridge

SEQ 1 FVNQHLCGSH LVEALYLVCG ERGFFYTPKT

SEQ 1 GIVEQCCTSI CSLYQLENYC N

MF C263 H394 N64 O76 S6

CI MAN

SR CA

LC STN Files: CA, CAPLUS, TOXLIT, TOXFILE

(1 REFERENCES IN FILE CA [illegible] TO DATE)

(1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA)

(1 REFERENCES IN FILE CAPLUS [illegible] TO DATE)

REFERENCE 1: [illegible]

REFERENCE 2: 129:1028

REFERENCE [illegible]

FAM 51,30,21
NTE multichain

type	------ location ------	description
bridge	Cys-7 - Cys-7'	disulfide bridge
bridge	Cys-19 - Cys-19'	disulfide bridge
bridge	Cys-6' - Cys-11'	disulfide bridge

SEQ 1 FVNQHLCGSH LVEALYLVCG ERGFFYTPKT

SEQ 1 GIVEQCCTSI CSLYQLENYC N
MF   C166 H889 N165 O51 S6
CI   MAN
CR   CA
LC   STN Files: CA, CAPLUS, CASREACT, TOXLIT, WPIATFULL
               3 REFERENCES IN FILE CA (1967 TO 2018)
               3 REFERENCES IN FILE CAPLUS (1967 TO 2018)

REFERENCE 1: [illegible]

REFERENCE 2: [illegible]

REFERENCE 3: [illegible]

L66 ANSWER 51 OF 55 REGISTRY COPYRIGHT 2018 ACS
RN   120177-51-7 REGISTRY
CN   Insulin (cattle), NA-[(1,1-dimethylethoxy)carbonyl]-eA-L-threonine-luA-L-isoleucine-29B-[N6-[(1,1-dimethylethoxy)carbonyl]-L-lysine]-2vB-D-L-alanine- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   3,4,44,45,90,91-Hexathia-[illegible],11,14,17,21,24,26,29,33,36,38,41,47,51,54,57,[illegible],63,66,69,72,75,78,81,84,86-hexaazaundecahexacyclo[72.11.7]dononacontane, cyclic peptide deriv.
CN   Insulin (ox), NA-[(1,1-dimethylethoxy)carbonyl]-eA-L-[illegible]-L-
FS   PROTEIN SEQUENCE
SQL 50,29,21
NTE multichain
     [illegible]

type	------ location ------	description
bridge	Cys-[illegible] - Cys-[illegible]	disulfide bridge
bridge	Cys-[illegible] - Cys-[illegible]	disulfide bridge
bridge	Cys-[illegible] - Cys-[illegible]	disulfide bridge

[illegible]

SEQ 1 [illegible]

SEQ 1 [illegible]
MF   [illegible]
CI   MAN
CR   CA
LC   [illegible]
[illegible]

CN [A-21A-chain, 1B-29B-insulin (human)] (9CI) (A INDEX NAME)
OTHER CA INDEX NAMES:
CN 3,4,44,45,46,47-Hexathia-6,11,14,17,20,23,26,29,32,35,38,41,42,43,48,
    49,50,51,52,53,54,55,56,57,58,59,60,61,62,63,64,65,66,67,68,69,70,71,
    cyclic peptide deriv.
CN Insulin (ox), 8A-L-threonine-10A-L-isoleucine-30B-L-alanine-
OTHER NAMES:
CN Des-alanine-B30-insulin (porcine)
CN Des(B 30)-alanine-pig insulin
CN Des(B30)-insulin (human)
CN Des-B30-alanine-insulin (porcine)
CN Desalanine-(B30)-porcine insulin
FS PROTEIN SEQUENCE
MW 50,29,21
NTE Additional

Type	------ Location ------	Description
bridge	Cys-7 - Cys-7'	disulfide bridge
bridge	Cys-19 - Cys-20'	disulfide bridge
bridge	Cys-6' - Cys-11'	disulfide bridge

SEQ 1 FVNQHLCGSH LVEALYLVCG ERGFFYTPK

SEQ 1 GIVEQCCTSI CSLYQLENYC N
DR 121796-35-8, 130987-81-4, 132022-05-1, 134657-89-4, 147203-42-3,
    74870-09-6, 78642-50-9, 144637-10-1, 9015-73-9, 81054-03-3, 84656-71-1,
    24528-78-3, 289054-43-9
MF C253 H376 N64 O75 S6
CI MAN
LC STN Files: CA, CAPLUS, CASREACT, MEDLINE, PIRLIT, USPATFULL
            87 REFERENCES IN FILE CA (1967 TO DATE)
             4 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
            87 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: [illegible]

REFERENCE 2: 133:99679

REFERENCE 3: 131:[illegible]

REFERENCE 4: 131:63464

REFERENCE 5: [illegible]

REFERENCE 6: [illegible]

REFERENCE 7: [illegible]

REFERENCE 8: [illegible]

REFERENCE 9: [illegible]

REFERENCE 10: [illegible]

[illegible]

CN Human Insulin
CN Humulin
CN Humulin R
CN Insulin (Cercopithecus aethiops)
CN Insulin (Macaca fascicularis)
CN Insulin (Macaca mulatta)
CN Insulin (Pan troglodytes)
CN L-Threonine, L-phenylalanyl-L-valyl-L-asparaginyl-L-glutaminyl-L-histidyl-L-leucyl-L-cysteinylglycyl-L-seryl-L-histidyl-L-leucyl-L-valyl-L-.alpha.-glutamyl-L-alanyl-L-leucyl-L-tyrosyl-L-leucyl-L-valyl-L-cysteinylglycyl-L-.alpha.-glutamyl-L-arginylglycyl-L-phenylalanyl-L-phenylalanyl-L-tyrosyl-L-threonyl-L-prolyl-L-lysyl-, cyclic (7.fwdarw.7')(11.fwdarw.11')-bis(disulfide) with glycyl-L-isoleucyl-L-valyl-L-.alpha.-glutamyl-L-glutaminyl-L-cysteinyl-L-cysteinyl-L-threonyl-L-seryl-L-isoleucyl-L-cysteinyl-L-seryl-L-leucyl-L-tyrosyl-L-glutaminyl-L-leucyl-L-.alpha.-glutamyl-L-asparaginyl-L-tyrosyl-L-cysteinyl-L-asparagine cyclic (6'.fwdarw.11')-disulfide
CN Novolin R
CN Penfil R
CN Ultraphane
FS PROTEIN SEQUENCE
SQL 51,30,21
NTE multichain

type	------ location ------			description
bridge	Cys-7	-	Cys-7'	disulfide bridge
bridge	Cys-19	-	Cys-20'	disulfide bridge
bridge	Cys-6'	-	Cys-11'	disulfide bridge

SEQ 1 FVNQHLCGSH LVEALYLVCG ERGFFYTPKT

SEQ 1 GIVEQCCTSI CSLYQLENYC N
MF C257 H383 N65 O77 S6
CI COM, MAN
DS STN files: AGRICOLA, AIDSLINE, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DIOGENES, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IFICDB, IFIPAT, IFIUDB, IMSDIRECTORY, IPA, MEDLINE, MRCK*, PROMT, PTECH*, TOXLINE, TOXNET, USAN, USPATFULL, ZDB
('File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)
[illegible] REFERENCES IN FILE CA (1967 TO DATE
[illegible] REFERENCES TO M.N.-[illegible] (RELATIVE) IN FILE CA
[illegible] REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: [illegible]

REFERENCE 3: [illegible]

REFERENCE 4: [illegible]

REFERENCE 5: [illegible]

REFERENCE 1: [illegible]

=> d ide can 139

L39 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS
RN 23713-49-7 REGISTRY
CN Zinc, ion (Zn2+) (9CI, CI) (CA INDEX NAME)
OTHER NAMES:
CN Zinc cation
CN Zinc dication
CN Zinc divalent ion
CN Zinc ion
CN Zinc ion(2+)
CN Zinc(2+)
CN Zinc(II)
CN Zinc(II) cation
CN Zinc(II) ion
CN Zn2+
MF Zn
LC STN Files: AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CEN, CIN, COMPENDEX, DETHERM*, EMBASE, IFICDB, IFIPAT, IFIUDB, MEDLINE, PIRA, PROMT, TOXCENTER, TOXLIT, USPATFULL, VETU
(*File contains numerically searchable property data)

Zn^{2+}

3674 REFERENCES IN FILE CA (1967 TO DATE)
17 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
3090 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:100169

REFERENCE 2: 134:100165

REFERENCE 3: 133:367079

REFERENCE 4: [illegible]

REFERENCE 5: [illegible]

REFERENCE 6: [illegible]

REFERENCE 7: [illegible]

REFERENCE 8: [illegible]

```
CN    F [illegible]
CN    F [illegible] (Metal)
CN    F [illegible]
CN    F 2000
CN    F 2000 (Metal)
CN    LC 3
CN    LC 3 (Element)
CN    LS 4
CN    LS 4
CN    LS 4 (Metal)
CN    NC-Zinc
CN    Rhodinsk
CN    TF
CN    TF (Metal)
CN    VM 4Flo
DR    1278[illegible]-[illegible]-2, 1951[illegible]-[illegible]-4, [illegible]-[illegible]-[illegible]-[illegible]-[illegible]
ED    Jr.
CI    COM
LC    STN Files:   AGRICOLA, AIDSLINE, ANABSTR, APILIT, APILIT2, APIPAT,
        APIPAT2, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CAPREVIEWS, CASREACT, CBNB, CEN, CHEMSAFE, CHEMINFORM*, CHEMLIST, CHEMSAFE,
        CIN, CSCHEM, CSNB, DETHERM*, DIOGENES, DIPPR*, DRUGU, EMBASE,
        HSDB*, IFICDB, IFIPAT, IFIUDB, INSPECTORY, IPA, MEDLINE, MRCK*,
        MSDS-OH*, NAPRALERT, NIOSHTIC, PIRA, PROMT, RTECS*, TOXLINE,
        TOXLIT, TULSA, ULIDAT, USPATFULL, VETU, VTB
          (*File contains numerically searchable property data)
        Other Sources:   DOE**, EINECS**, TSCA**
          (**Enter CHEMLIST File for up-to-date regulatory information)


Zn

          [illegible] REFERENCES IN FILE CA [illegible] TO DATE
           10306 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
          [illegible] REFERENCES IN FILE CAPLUS [illegible] TO [illegible]
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REFERENCE  10:  [illegible]
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